May 7, 2024

Sarah K. Emond, MPP
President and Chief Executive Officer
Institute for Clinical and Economic Review
Two Liberty Square, Ninth Floor
Boston, MA 02109

Dear Ms. Emond,

The Partnership to Improve Patient Care (PIPC) appreciates the opportunity to comment on the Institute for Clinical and Economic Review (ICER) assessment on chronic obstructive pulmonary disease (COPD).

COPD impacts almost 16 million Americans. It is a highly heterogeneous condition, which can make it challenging to treat.\(^1\) Given this reality, it is important that ICER accurately capture the value of new treatments, as segments of the patient population still desperately need new options. We encourage ICER to consider the following comments.

**ICER’s sources of data do not accurately capture the reality for COPD patients in the United States.**

ICER’s choice of data for costs per exacerbation appear to underestimate the true cost of exacerbations in the United States. The ICER model uses a single study that found the cost of moderate exacerbation estimated at $2,415 and a severe exacerbation at $26,047. This study relies on a sample of 300,000 patients. A much larger recent study that utilized data from CMS\(^2\) suggested a range of cost per exacerbation of between $26,544 - $43,774 based on category of severity. This data relied on a much larger sample size of just under four million patients. In this instance, the more recent study with a larger sample population appears to provide more credible data. We would suggest that, where available, ICER should be using the most recent and largest studies.

We are also concerned that the sources used for mortality modifiers by COPD severity may underestimate the years of life lost due to COPD. The ICER model assumes standardized mortality ratios compared to those without COPD as 1.3 for moderate, 1.6 for severe and 1.9 for very severe.\(^3\) The original source is a European study using Eurostat data from 21 countries, and states that the measures of severity varied widely by country. The paper itself is a request to improve standardization of outcome measures in COPD. There is a better source for mortality

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\(^1\) [https://www.copdfoundation.org/What-is-COPD/Understanding-COPD/What-is-COPD.aspx](https://www.copdfoundation.org/What-is-COPD/Understanding-COPD/What-is-COPD.aspx)


ratios that is based on United States data.4 This study estimates standardized mortality ratios compared to those without COPD as 1.6 for moderate COPD and 2.7 for severe COPD. As ICER’s assessments are conducted for an American audience and meant to drive decision making within the United States health care system, the paper based on United States data would be the more accurate source.

Finally, ICER’s health state utility values are derived from a randomized clinical trial when real world data is available and more accurate. ICER uses utility scores of 0.787 for moderate, 0.750 for severe and 0.647 for very severe COPD. These are second hand and taken from a multi-center randomized clinical trial (RCT) using the UK value set5. Over the years, PIPC has laid out the many limitations that result from using utility data derived solely from the trial setting. RCT populations are generally much healthier than real-world disease-specific populations.6 There are always explicit and implicit exclusion criteria for recruitment into trial settings,7 including age, the existence of co-morbidities8 and levels of healthcare access and utilization, that make RCT populations rarely representative of real-world populations of need.9,10

In addition, utilities in RCTs tend to be inflated compared to non-RCT samples of patients11 as EQ5D gains are often generated for patients in RCTs that are non-disease or treatment related socio-emotive components, that can occur because of receiving greater care and attention from healthcare professionals. There is also a placebo effect from patients in both arms of the trial. Numerous studies have highlighted the utilities generated in RCTs are generally much higher than the equivalents would be for a real-world population.12

Ultimately, ICER should be looking to use the best possible sources that are most representative of the population in need of treatment. This should include prioritizing sources based on United States data, large sample sizes, real-world data, and the most recent publications.

Evidence suggests that frequency of exacerbations is related to significantly worse survival outcomes, a dynamic that is not captured in ICER’s model.

Exacerbations, whether treated or untreated, have a detrimental and prolonged impact on patients’ health status and outcomes, and have cumulative negative effects on lung function over time. COPD exacerbations are highly heterogeneous, varying in severity and phenotype. Evidence has shown that exacerbations are related to worse survival outcomes, yet the model only bases risk of mortality modifiers on severity level, not rate of exacerbations. The frequency of exacerbations is also a marker of both disease burden and mortality risk. Frequent exacerbations, mainly in patients with severe COPD, accelerate disease progression and mortality. This is a dynamic also ignored in the ICER model.

Exacerbations of COPD also have a cumulative effect on lung function. Patients in the 3-year TORCH study who experienced 0–1.0 moderate to severe exacerbations per year had a 37% faster decline in lung function than those with no exacerbations. Among those patients who experienced more than one moderate to severe exacerbation, the rate of decline in lung function was 65% faster. Rate of exacerbations also varies strongly not just by severity but also by age and gender, the dynamic nature of which is not adequately represented using a single estimate of exacerbations per cycle used in the model.

The ICER model largely ignores the complexity of this dynamic between lung function and exacerbation rate over time, and the impact of exacerbation rate on mortality and disease progression. This is a stark omission, as it will not allow ICER’s assessment to capture an accurate value of treatment of COPD.

ICER Continues to Use the Discriminatory QALY and the Similar Measure evLYG.

Multiple studies have shown that cost-effectiveness models using the quality-adjusted life year (QALY) discriminate against patients with chronic conditions, like COPD, and people with disabilities. There is widespread recognition that the use of the QALY is discriminatory,
reflected in laws that bar its use in government decision-making. The National Council on Disability (NCD), an independent federal agency advising Congress and the administration on disability policy, concluded in a 2019 report that QALYs discriminate by placing a lower value on treatments which extend the lives of people with chronic illnesses and disabilities. NCD recommended that policymakers and insurers reject QALYs as a method of measuring value for medical treatments.

Additionally, we share the concerns of NCD about the equal value of life year gained (evLYG), a similar measure created by ICER to supplement the QALY. The evLYG is a simplistic fix attempting to address criticism that the QALY devalues life years lived with a disability, yet it fails to account for oversimplified measures of quality-of-life gains in expected life years (not extended life years) and it does not account for any health improvements in extended life years. Like the QALY, the evLYG relies on average estimates based on generic survey data and obscures important differences in patients’ clinical needs and preferences, particularly those with complex diseases and from underrepresented communities. It assumes that people value life year gains more than quality of life improvements, giving a lower value to health interventions in patient populations that have a lower life expectancy or fewer life years gained from treatment, which may include people with disabilities, underlying chronic conditions, the elderly, and certain communities of color. With the evLYG and the QALY, ICER promotes two compromised and flawed measures of health gain. Deciding which to choose is confusing and inconsistent.

ICER fails to capture the heterogeneous nature of COPD.

As ICER notes in its report, COPD is a widely heterogenous disease both in terms of the cause, the level of comorbidity, and its impact on patient experience. This points to a larger issue with respect to value assessment reporting that the archetypal cost-effectiveness model relies heavily on producing effect size based on population averages, and rarely are results specific to subpopulations released in results. It is well established that generating and reporting of

differential value assessment across subgroups leads to substantial health gains, both through treatment selection and coverage.\textsuperscript{29,30}

If ICER is to take seriously its role of informing health policy decision makers about the value of new therapies, it needs to move away from the assumption that all patients are the same. No patient is average, and it is essential that ICER moves to acknowledge this and incorporate analysis of subpopulations and produce ranges of value rather than relying on an archetypal patient.

**Conclusion**

PIPC urges ICER to reconsider both its data sources and modeling choices if it seeks to provide an accurate representation of value to patients with COPD. Where available, real-world evidence based on United States populations should be relied on in the model. ICER must also move away from using discriminatory metrics and the antiquated practice of looking at value to an “average” patient.

Sincerely,

\[\text{\underline{Coelho}}\]

Tony Coelho  
Chairman  
Partnership to Improve Patient Care